Effect of Maternal Antibody Upon Vaccination With Infectious Bovine Rhinotracheitis and Bovine Virus Diarrhea Vaccines

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ABSTRACT

This report presents the normal rate of decay of maternal antibody and the influence of maternal antibody on responses to a single vaccination with modified-live bovine virus diarrhea and infectious bovine rhinotracheitis virus vaccines at 196 days of age and on response to vaccinations with the same vaccines given twice at 84 and 196 days of age. Passive immunity decreased to near zero over the first six months of life for both bovine virus diarrhea and infectious bovine rhinotracheitis controls. All calves seroconverted to bovine virus diarrhea vaccine at 84 days of age, even though high levels (> 1:32) of maternal antibodies were present. These calves did not seroconvert to infectious bovine rhinotracheitis vaccine at 84 days of age when high levels (< 1:16) of maternal antibodies were present. Calves responded well to bovine virus diarrhea and infectious bovine rhinotracheitis vaccines given only once at 196 days of age after passive immunity disappeared. Calves which were revaccinated with infectious bovine rhinotracheitis seroconverted showing a more rapid response than the single vaccinates. Those revaccinated with bovine virus diarrhea showed an immediate response of small magnitude.

RÉSUMÉ

Ce rapport présente le taux de déclin normal des anticorps maternels et son influence sur la réponse des veaux à une seule injection d'un vaccin atténué contre la diarrhée à virus bovine et d'un autre contre la rhino-trachéite infectieuse bovine, à l'âge de 196 jours, ainsi qu'à deux injections de ces deux vaccins, à l'âge de 84 et 196 jours. L'immunité passive à l'égard des deux maladies précitées se dissipa presque complètement, durant les six premiers mois de la vie, chez les veaux témoins. Tous les veaux vaccinés contre la diarrhée à virus bovine, à l'âge de 84 jours, développèrent des anticorps, même s'ils affichaient encore un taux d'anticorps maternels supérieur à 1:32, mais ils n'en développèrent pas à l'endroit de la rhino-trachéite infectieuse bovine, lorsque leur taux d'anticorps maternels était supérieur à 1:16. Les veaux réagirent favorablement à une seule vaccination contre les deux maladies précitées, à l'âge de 196 jours, après la disparition de leur immunité passive. Les veaux revaccinés contre la rhino-trachéite infectieuse bovine développèrent des anticorps plus rapidement que ceux qui ne reçurent qu'une seule injection de vaccin. Les veaux revaccinés contre la diarrhée à virus bovine réagirent immédiatement, mais plus faiblement.

INTRODUCTION

The value of maternal antibody transferred to the newborn calf by nursing of colostrum is well known and is recognized as an essential management practice (1,2). It is through this initial feeding of colostrum that the newborn receives natural protection against pathogens to which it is immediately exposed. However, passively administered antibody for certain antigens like tetanus toxoid (3), diptheria toxin (4) and polio virus (5) acts to inhibit production of antibody to antigen. The degree of suppression is influenced by the intensity of antigenic stimulation and the dissociation of the antigen antibody complex *in vivo* (6). Despite the lack of a primary antibody response it has been shown that some sensitization of memory cells or priming for a secondary response does occur (7,8).

The effect of passive antibody on the active immunization of the calf with bovine virus diarrhea (BVD) and infectious bovine rhinotracheitis (IBR) modified-live virus (MLV) vaccines is not completely understood. Immunization of calves with passive antibody present using two vaccinations of BVD-MLV resulted in seroconversion in one study (9). Concern was raised in this study that because no control animals were included in the group, active immune stimulation may have been the result of a field virus. Another study in a herd with endemic BVD was unable to induce seroconversion before three months of age despite repeated vaccination prior to this time (10). Immunization of calves with IBR-MLV in the face of passive immunity appears to require complete absence of passive antibodies for seroconversion to occur (9,11). Early immunization series in animals with passive immunity present using more than one vaccination with IBR-MLV may sensitize the immune system (9). It is not known if this can also be done more economically using a single IBR vaccination.

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There is obviously a need for more information on the effect of passive immunity on active immune stimulation because management practices with both beef and dairy cattle make early immunization desirable. This is paricularly true in beef herds which practice preconditioning, where the calf is vaccinated with BVD and IBR vaccines prior to weaning. Vaccination in the presence of antibody may also be beneficial for calves in herds with endemic BVD or IBR. These vaccinations may be capable of producing enough antigenic stimulus to overcome passive immunity or at least sensitize specific memory cells before the calves become completely devoid of BVD or IBR antibodies and thus highly susceptible to infection with field virus.

The purposes of this study were to observe the normal rate of decline of BVD and IBR antibody in control calves without exposure to vaccine or field virus and relate this to the effects of administering single vaccinations of IBR-MLV and BVD-MLV at specific times to calves with maternal antibody present.

MATERIALS AND METHODS

ANIMALS

Thirty-six beef calves (males and females) were used in this study. Calves were divided into three groups. Group A consisted of 13 calves vaccinated at 84 and 196 days of age against BVD and IBR. Group B consisted of 14 calves vaccinated at 196 days of age against BVD and IBR. A control group (C) consisted of nine calves which remained unvaccinated. Some of the control calves were housed with each of the vaccination groups. The calves were raised with their dams in a dry lot facility till they were weaned at 120 days. After weaning they were again placed in similar dry lot facilities with open pens and pole barns for shelter.

VACCINATION

Dams of all calves had been vaccinated at least two times intramuscularly with IBR-MLV and BVD-MLV vaccines (Resbo IBR and Resbo BVD, Norden Laboratories, Lincoln, Nebraska). Calves in groups A and B were vaccinated intramuscularly one and two times respectively, with both IBR-MLV and BVD-MLV.

BLOOD SAMPLES

Blood samples were collected when the calves had attained maximum maternal antibody at 48 hours of age. After that, samples were collected from each animal once every four weeks for eight months. In addition samples were collected at weekly intervals for two weeks after vaccination. Nonvaccinated controls were also bled on an identical schedule. Blood samples (10 mL) were collected from the jugular vein using a 20-gauge hypodermic needle attached to a sterile tube (partial vacuum). The samples were allowed to stand until clot retraction had occurred. These were centifuged at 600 x g for ten minutes, and serum was collected to conduct serum neutralization (SN).

SERUM NEUTRALIZATION

The standard microtiter SN was used to determine the antibody titer for BVD and IBR. To eliminate laboratory variation, the SN was conducted for BVD and IBR on all serum samples from a single animal at one time. Fetal bovine turbinate cells were employed for the SN test with a cytopathogenic strain of BVD virus, Singer strain 300 $TCID_{50}$/0.1 mL and IBR virus, Colorado strain 300 $TCID_{50}$/0.1 mL (Singer strain and Colorado strain obtained from National Veterinary Services Laboratory, Ames, Iowa). The endpoint antibody titer was expressed as the reciprocal of the highest twofold serial dilution of serum that completely inhibited viral growth as indicated by cytopathic effect. Data are presented showing the reciprocal of the GM titer for each group of calves. Also, titers are expressed as the $\log_2$ of the reciprocal GM titer.

STATISTICAL ANALYSIS

The slopes of the lines representing the decay of colostral BVD and IBR titers in the nonvaccinated controls were compared using Student's t-test. Response to vaccination for each vaccine was evaluated based on its ability to induce seroconversion (fourfold rise in titer). Differences in the rate and magnitude of response between groups were determined by comparing the GM titers at specific time points using Student's t-test.

RESULTS

In the control group (Fig. 1) the GM titer for BVD antibodies was 1:692 at two days of age, at which point it began to decay. There was a steady decline until titers reached 0 at 200 days. The GM titer for IBR antibodies at two days was 1:32, at which time it started to decay with a steady decline until antibody titers reached 0 (around 170 days). The rate of decay for BVD antibody titers was more rapid than for IBR antibody titers. The slopes of the two lines differed significantly ($P < 0.05$). However, because the initial titer of IBR was lower, the calves lost their maternal immunity to IBR before BVD. If the titers of all the calves prior to the time of the first vaccination are averaged to give a mean slope for the decay of colostral antibodies to IBR and BVD it was found the lines were identical. The average half-life ($t_{1/2}$) was found to be 19 days for IBR and 20 days for BVD. No unexpected rise in titer to IBR or BVD virus occurred in the control calves.

Calves given BVD vaccine at 84 days had a GM titer for BVD of 1:35 at that time. Following immunization, antibody titers decreased at a similar rate for two weeks reaching a titer of 1:22. At this time the calves seroconverted and reached a peak GM titer of 1:388 at 168 days of age. At 196 days calves were revaccinated. These revaccinated animals had an immediate rise in antibody titer of small magnitude with a subsequent gradual decline (Fig. 2).

Calves given IBR vaccine at 84 days of age had a GM titer of 1:19. Rather than seroconverting after vaccination, antibody titers steadily decreased (Fig. 3). However following revaccination at 196 days of age, antibody titer to IBR increased immediately, seroconverting and reaching a GM titer of 1:10 at 210 days of age.

In vaccinated group B, calves given the BVD vaccination at 196 days of age showed a GM titer of 1:1. Two weeks after immunization, calves

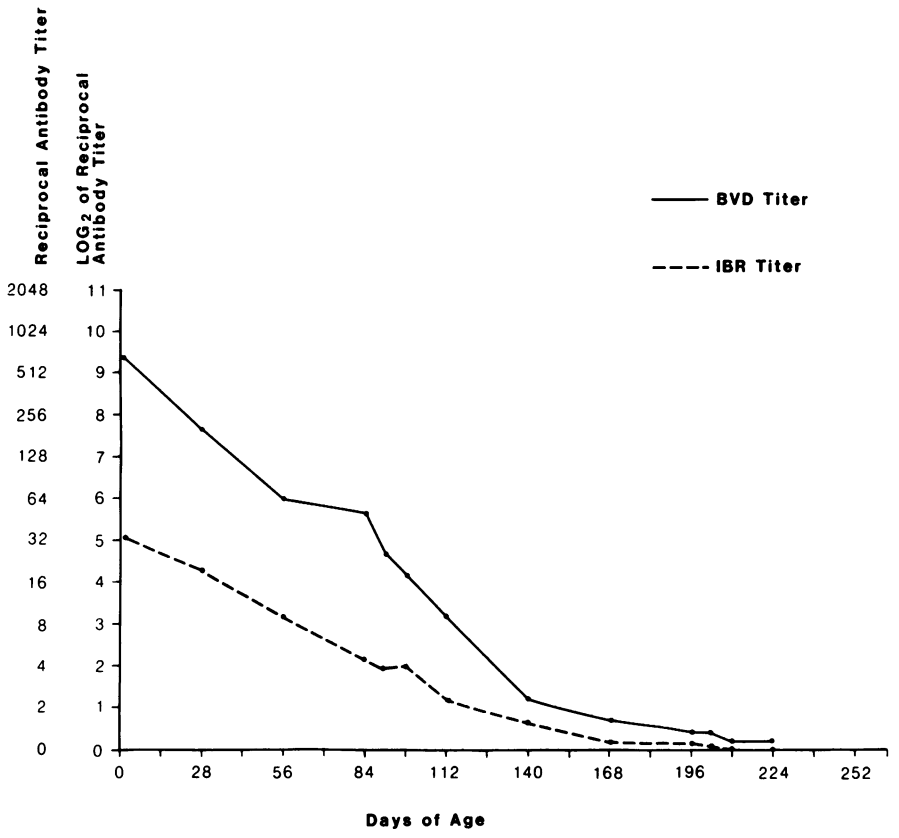

Fig. 1. The decay of maternal antibodies to BVD and IBR virus in unvaccinated calves.

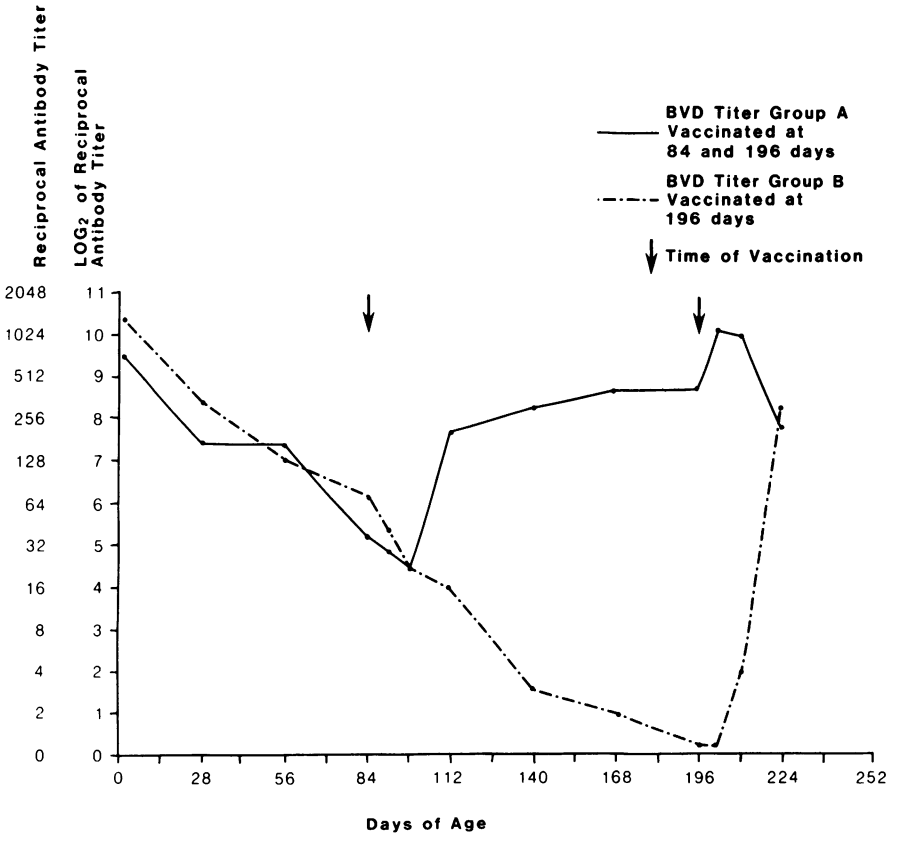

Fig. 2. Serological response of calves given a single BVD vaccination (Group B) and two BVD vaccinations (Group A).

seroconverted and attained a peak GM titer of 1:287 at four weeks (Fig. 2). Calves given IBR vaccine at 196 days of age had a GM titer of 1:1. One week after immunization they had no rise in antibody titer to IBR. However, they seroconverted and attained a peak GM titer of 1:10 at 14 days after immunization (Fig. 3).

The vaccine response at 196 days was different for the two groups with both IBR and BVD. With BVD-MLV vaccine only group B, the unvaccinated group, seroconverted. Group A, the previously vaccinated group, failed to seroconvert but did show an immediate rise in titer within one week. The group B calves took three weeks to achieve a response equal to the group A calves and at one and two weeks the titer was significantly ($P < 0.05$) lower. The IBR antibody response was of equal magnitude for both groups at two weeks after vaccination, however, at one week postvaccination the previously vaccinated calves in group A had a significantly ($P < 0.05$) higher titer than did the calves of group B.

DISCUSSION

Examination of BVD titers in unvaccinated animals show that the maternal antibodies decreased steadily to 0 by 200 days of age. This finding concurs with other studies that show antibody titers decay to undetectable levels by 105 to 230 days (1,12,13). The lack of active immune stimulation evidenced by rising titers in these control animals was a good indication that all calves remained free of IBR or BVD infection in this study.

The rate of decay for BVD was more rapid than IBR in the controls. When a larger number of calves was included in the calculation this difference disappeared indicating it was an artifact caused by the small number of controls. The decay of colostral antibody for both IBR and BVD agreed well with the findings of Brar (9) as well as what is known about colostral IgG in general (1).

In this study, calves given BVD vaccine at 84 days of age, in the presence of maternal antibody, seroconverted within two weeks. In contrast, calves failed to seroconvert after immunization with IBR at 84 days, although

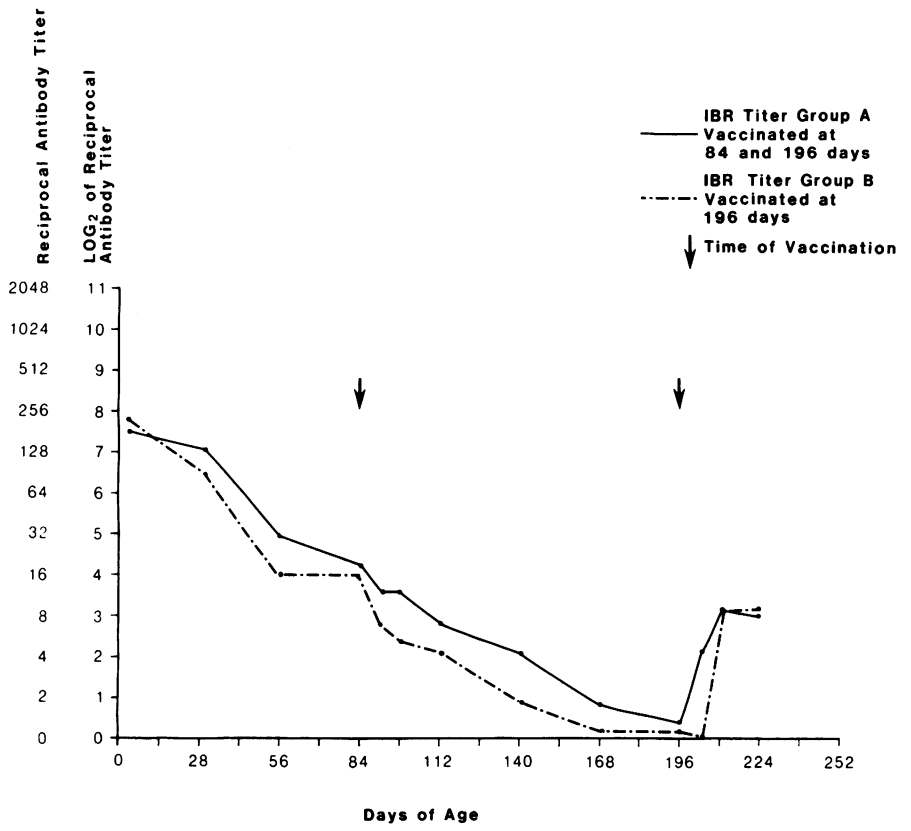

Fig. 3. Serological response in calves given a single IBR vaccination (Group B) and two IBR vaccinations (Group A).

maternal antibody titers were lower than for BVD. However, when revaccinated at 196 days with BVD and IBR, calves immediately seroconverted to IBR with high titers, indicative of an anamnestic response. The calves also responded to BVD vaccine immediately following vaccination but with only a slight increase in antibody titer. This poor response to BVD may be a result of the existing high titer against BVD. Calves given BVD and IBR vaccine only at 196 days of age seroconverted to both BVD and IBR after two weeks.

The results from IBR vaccination agree with previous work that showed passive immunity, in addition to protecting against naturally occurring infection, inhibits the formation of active immunity from live-virus vaccine administered intramuscularly (9,11,14). In this study, maternal antibodies interfered with antibody production to a single IBR-MLV vaccination at 84 days of age. However, following the second vaccination the calves displayed an apparent anamnestic response as evidenced by a more rapid rise in titer. These results support the results of Brar *et al* (9) that showed an initial series of vaccination was able to prime the immune system to respond to IBR (memory cells) although no detectable seroconversion was observed after primary vaccination. In contrast, the single BVD-vaccinated calves seroconverted at 84 days of age indicating that maternal antibodies did not interfere with vaccination at that age. The fact that BVD-MLV vaccine is capable of stimulating seroconversion in the face of passive immunity when IBR-MLV vaccine is not, suggests the BVD vaccine has a greater antigenic stimulus.

This study shows it may be possible to confer protection through the use of IBR and BVD vaccines at an early age after initial high levels of passive antibody have declined. The average level of antibody produced by early vaccination for BVD in this study has previously been shown to be protective (15). With IBR, researchers have felt that any level of serum neutralizing antibody is protective (16). Although none was produced, the sensitization or priming of memory cells by the initial IBR vaccination may be of value. A more rapid secondary humoral response could then occur upon challenge with field virus as was observed with the second vaccination in this study and in the study of Brar *et al* (9). However, this may also be an indication that cell-mediated immunity to IBR has been stimulated although this was not evaluated in this study. Calves recovered from respiratory infection with a virulent strain of IBR have been shown to be immune to subsequent challenge even though they had no detectable serum antibody (17). It has been shown with intranasal challenge that strong cell-mediated immunity can exist with minimal humoral immunity (18). Cell-mediated immunity may also play an important role in protection against IBR in conjunction with humoral immunity (19).

The efficacy of either of these vaccines as part of early vaccination in calves would be modified by the existing level of passive immunity and by the challenge dose of field virus. Vaccination programs in calves for both IBR (20) and BVD (10) in herds where these diseases were endemic have not been of obvious benefit. The desired effects of such vaccination programs would have to be weighed against the possibility of the early immunization program acting as a stressor predisposing the animals to secondary problems as has been observed in other studies (21,22).

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